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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/246,307	02/08/99	KOZIKOWSKI	A 9928-0009-99
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HM12/0621

EXAMINER

GUPTA, A

ART UNIT

PAPER NUMBER

1653

DATE MAILED:

06/21/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.
09/246,307

Applicant(s)
Kozikowski et al.

Examiner
ANISH GUPTA

Group Art Unit
1653



☒ Responsive to communication(s) filed on Jun 2, 2000

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire three month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-7, 10-17, 20-28, 31, and 32 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-7, 10-17, 20-28, 31, and 32 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been
☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Election/Restriction

1. Applicant's election without traverse of Group I, claims 1-32, 71 and 72 in Paper No. 6 is acknowledged.
Applicant's election without traverse species (2a) for initial examination on the merits is also acknowledged.
Claims 1-7, 10-17, 20-28, 31, and 32 read on the elected species.
2. Claims 8-9, 18-19, 29-30, 33-72 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 6.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 11-17, 20-28, and 31-32 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

(1) The nature of the invention:

The invention is drawn to, as one of its embodiments, a method of treating neurological disorders including Alzheimer's, treatment of CNS injury and enhancement of cognitive function using 2,5-diketopiperazines compounds.

(2) The state of the prior art

The state of the art for Alzheimer's disease can be summed up by the Patel reference, which teach that Alzheimer's disease is known to be difficult to treat and that there is neither a clear understanding of the origin and pathophysiology of the disease nor an animal model of illness (see page 81). Furthermore, it is well established in the art that acetylcholine transmitting neurons and their target nerve cells are particularly affected. Even a therapeutic strategy involving replacement or enhancement of acetylcholine within the brain would probably not halt the progression of Alzheimer's disease (see page 2136). In conclusion, Patel states that the search for an effective cognition-enhancing therapy has so far proved elusive.

Moreover, the art has also recognized the ineffectiveness of therapeutics on the regeneration of motor neurons after a CNS injury.

(3) The relative skill of those in the art

The relative skill of those in the art is high.

(4) The predictability or unpredictability of the art

Considering that Alzheimer's disease is known to be difficult to treat and that there is neither a clear understanding of the origin and pathophysiology of the disease nor an animal model of illness and that the search for an effective cognition-enhancing therapy for AD has so far proved elusive, the unpredictability of treatment and prevention of Alzheimer's is very high. For the treatment of neurological disorders, where there involves the regeneration of motor neurons, the art is similarly unpredictable.

(5) The breadth of the claims

The claims are to a method of treating neurological disorders and enhancing cognitive function by the administration of drawn to various diketopiperazines compounds. The claims are drawn to a method of treatment of CNS injury and neurological disorders, which is inclusive of regeneration of neurons.

(6) The amount of direction or guidance presented and (7) The presence or absence of working examples

The specification provides in vivo tests motor functions following fluid percussion injury. In this type of injury, a gradual recovery of function occurs over an extended time period of 2-3 weeks. The specification also provides tests of spatial memory. However, the specification does not provide ample guidance to allow for the treatment of all neurological disorders and CNS injuries as claimed. Although the specification has provided guidance on motor neurons that have been injured and have the ability to gradually recover, the specification has not provided any guidance on the effectiveness of the compounds on motor neurons that do not have the ability to recover which is a characteristic of neurological disorders such as ALS and spinal cord injuries. Working examples for these disorders are necessary there exists an intrinsic inability of CNS neurons to mount a regenerative response. For Alzheimer's disease, the art has indicated that to date, there is neither a clear understanding of the origin and pathophysiology of Alzheimer's Disease nor an animal model of the illness. This is also evidence of the extreme difficulty and unpredictability in treatment of Alzheimer's Disease. In the instant specification, there is very little guidance provided in the way of working examples that the claimed compounds would be effective in the treatment of Alzheimer's. The specification does not provide an art recognized model that would clearly demonstrate that the compounds would be effective in the treatment of Alzheimer's. The art has not yet recognized effective cognition-enhancing therapy for AD, as summarized by Patel.

Moreover for the working examples, compounds 1-4 were tested in the motor test and compound 2 was tested for a spatial memory test. The specification does not provide examples that include the testing of other compounds, for example compound 7. It is well established that the applicants need not provide working examples in the specification for every embodiment. However, it is also established In cases involving unpredictable factors, such as most chemical reactions and physiological activity, more may be required. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970)

(contrasting mechanical and electrical elements with chemical reactions and physiological activity). See also In re Wright, 999 F.2d 1557, 27 USPQ2d 1510 (Fed. Cir. 1993); In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

(8) The quantity of experimentation necessary

Considering the state of the art and the high unpredictability and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to treat all types of neurodegenerative disorders and CNS injuries.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-7 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Stadler et al. (FR 1583797)

The claims are drawn to bicyclic 2,5-diketopiperazines and its derivatives.

The reference teaches a compound Spiro [cyclohexane-1,3'(4'H)-pyrrolo[1,2-a]pyrazine]-1',4' (2,H)-dione, tetrahydro-, (8'as)-, having the registry number 28385-25-3, that is similar to compound number 2(a), in claim 10. (See Chem. abstract and the corresponding structure).

4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anish Gupta whose telephone number is (703) 308-4001.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang, can normally be reached on (703) 308-0254. The fax phone number of this group is (703) 308-4242.

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Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Anish Gupta

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